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(21) International Application Number: PCT/US97/21803 (22) International Filing Date: 1 December 1997 (01.12.97) (30) Priority Data: 08/758,417 2 December 1996 (02.12.96) US (71) Applicant: GENPHARM INTERNATIONAL [US/US]; Suite C, 855 California Avenue, Palo Alto, CA 94304 (US). (72) Inventors: LONBERG, Nils; 930 Edgecliff Way, Redwood City, CA 94061 (US). KAY, Robert, M.; 2127 Broadway #5, San Francisco, CA 94115 (US). (74) Agents: APPLE, Randolph, T. et al.; Townsend and Townsend and Crew LLP, 8th floor, Two Embarcadero Center, San Francisco, CA 94111-3834 (US).			(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published With international search report.
(54) Title: TRANSGENIC NON-HUMAN ANIMALS CAPABLE OF PRODUCING HETEROLOGOUS ANTIBODIES			
(57) Abstract The invention relates to transgenic non-human animals capable of producing heterologous antibodies and methods for producing human sequence antibodies which bind to human antigens with substantial affinity.			

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**Hybridoma producing antibody specific for interleukin-8 - used to prevent
efflux of neutrophils from vasculature, and treat reperfusion injury**

Patent Assignee: GENPHARM INT (GENP-N)

Inventor: KAY R M; LONBERG N

Number of Countries: 078 Number of Patents: 003

Patent Family:

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WO 9824884	A1	19980611	WO 97US21803	A	19971201	199829 B
AU 9856881	A	19980629	AU 9856881	A	19971201	199845
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Abstract (Basic): WO 9824884 A

A hybridoma comprising a B cell obtained from a transgenic mouse having a genome comprising a human heavy chain transgene and a human light chain transgene, the B cell being fused to an immortalised cell to generate a hybridoma, where the hybridoma produces a detectable amount of an immunoglobulin that specifically binds interleukin-8 (IL-8), is new.

Also claimed are: (1) a composition comprising a substantially pure immunoglobulin produced by the above hybridoma; (2) a composition comprising a substantially pure human monoclonal antibody (MAb), where the Ab has an affinity constant (Ka) of at least $2 \times 10^9 \text{ M}^{-1}$ for binding human IL-8, and where the immunoglobulin consists of: (a) a human light chain sequence composed of: (i) a light chain variable region having a polypeptide sequence which is substantially identical to a polypeptide sequence encoded by a human V-L gene segment and a human J-L segment; and (ii) a light chain constant region having a polypeptide sequence which is substantially identical to a polypeptide sequence encoded by a C-L gene segment; and (b) a human heavy chain sequence composed of: (i) a heavy chain variable region having a polypeptide sequence which is substantially identical to a polypeptide sequence encoded by a human V-H segment optionally a D region and a human J-H segment; and (ii) a constant region having a polypeptide sequence which is substantially identical to a polypeptide sequence encoded by a human C-H gene segment; and (3) a method of suppressing a T-cell helper dependent immune response in a primate, comprising administering a therapeutically effective dose of a human monoclonal antibody having a Ka of at least $2 \times 10^9 \text{ M}^{-1}$ for binding human CD-4.

USE - The MAb can be used in a method for preventing efflux of neutrophils from vasculature in a patient. It can also be used in a method for treating reperfusion injury (both claimed). The CD4 binding Ab will be able to be used to reduce undesirable autoimmune reactions,

inflammatory responses and rejection of transplanted organs. The anti-IL-8 Abs can reduce tissue damage and prolong survival in animal models of acute adult respiratory distress syndrome (ARDS) and acid induced lung injury. The anti-IL-8 Abs can be used for the treatment of reperfusion injuries (especially to the lung and heart), vasculitis, septic shock, autoimmune diseases (including glomerulonephritis, inflammatory bowel disease, rheumatoid arthritis, and psoriasis), allergic reactions (e.g. asthma) and cystic fibrosis.

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Title Terms: HYBRIDOMA; PRODUCE; ANTIBODY; SPECIFIC; INTERLEUKIN; PREVENT; EFFLUX; TREAT; REPERFUSION; INJURY

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